Amendments to the Specification

Please substitute the abstract provided herein on a separate sheet, with the abstract previously submitted in this application.

Please insert the following section heading and paragraph immediately after the title:

CROSS-RELATION TO RELATED APPLICATIONS

This application is a 371 application of PCT/EP2005/003663, having an international filing date of April 7, 2005.

Please insert the following section heading immediately before paragraph [003] of the application as published (US 2007/0232658 A1):

BACKGROUND OF THE INVENTION

Please insert the following section heading immediately before paragraph [0064] of the application as published (US 2007/0232658 A1):

SUMMARY OF THE INVENTION

Please insert the following section heading immediately before paragraph [0065] of the application as published (US 2007/0232658 A1):

DETAILED DESCRIPTION OF THE INVENTION

Please insert the following immediately after paragraph [0092] of the application as published (US 2007/0232658 A1):

What is claimed is:

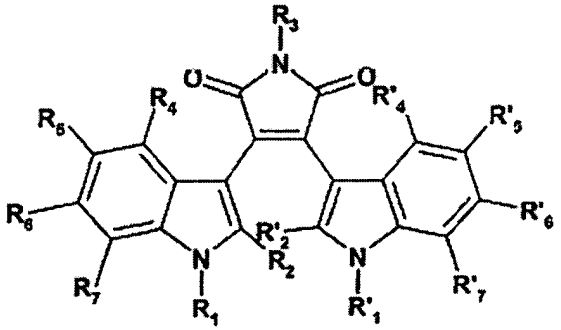
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method for treating ~~or preventing~~ organ or tissue transplant rejection or an autoimmune disease other than diabetes mellitus or for ~~preventing~~ treating graft-versus-host disease in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of a protein kinase C inhibitor of formula I, II, III or IV or a pharmaceutically acceptable salt, hydrate or solvate thereof,

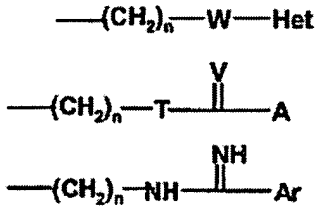
wherein compounds of formula I are



I

wherein

each of R_1 and R'_1, independently, is hydrogen, alkyl, haloalkyl, alkenyl, arylalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, acyl-aminoalkyl, acyloxyalkyl, cyanoalkyl, amidinoalkyl, carboxyalkyl, alkoxycarbonylalkyl, aminocarbonylalkyl, or a group of the formula (a), (b) or (c)



(a)

(b)

(c)

wherein Het signifies a heterocyclyl group; W signifies NH, S or a bond; T signifies NH or S; V signifies 0, S. NH, or NCN; A signifies alkylthio, amino, monoalkylamino or dialkylamino; Ar signifies aryl;

each of R_2 and R'_2, independently, is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, C_1-C_3alkylthio, $S(O)C_1$-C_3alkyl, CF_3;

or R_1 and R_2 form together $—(CH_2)_r—X—CH_2—$ wherein r is 1, 2, or 3, and X is CHR_8 or NR_8 wherein R_8 is $(CH_2)_sR_9$ wherein R_9 is hydrogen, hydroxy, alkoxy, amino,

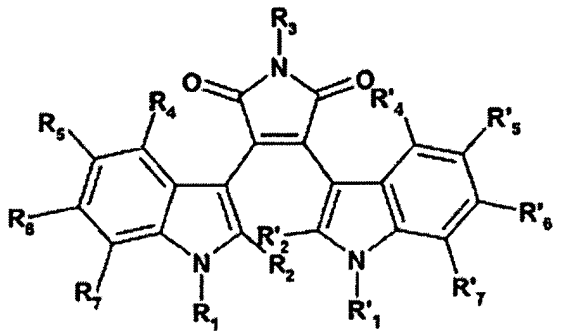
monoalkylamino, dialkylamino, trialkylamino, azido, acylamino, alkoxycarbonyl, cyano, amidino, or aminocarbonyl, and s is 0, 1, 2 or 3;

R_3 is hydrogen or CH_3CO;

each of R_4, R'_4, R_5, R'_5, R_6, R'_6, R_7 and R'_7, independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, —COO(C_1-C_3alkyl), CF_3, nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3alkylthio, or S(O)C_1-C_3alkyl; and

n is 1, 2, 3, 4, 5 or 6;

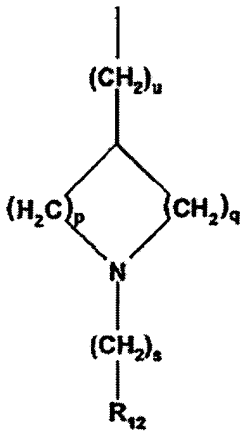
and compounds of formula II are



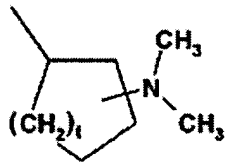
II

wherein

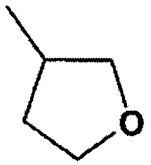
R_1 is a group of formula (d), (e) or (f)



(d)



(e)



(f)

wherein each of p and q independently is 1, 2, 3, or 4;

s is 0, 1,2 or 3;

t is 1 or 2;

u is 0 or 1; and

R_{12} is hydrogen, alkyl, haloalkyl, cycloalkyl, acetyl, aryl, --CH(aryl)$_2$, amino, monoaikylamino, dialkylamino, guanidino, —C(=N(alkoxycarbonyl))NH(alkyoxy-carbonyl), amidino, hydroxy, carboxy, alkoxycarbonyl or heterocyclyl;

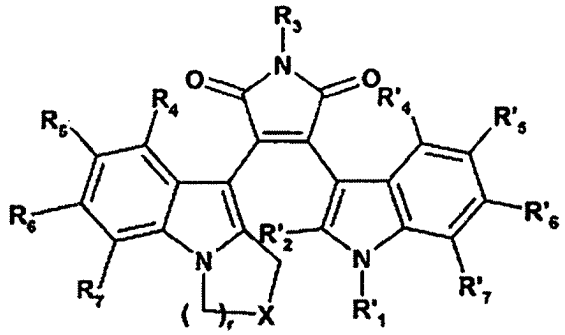
R'_1 is hydrogen, C_{1-4}alkyl, aminoalkyl, monoalkylaminoalkyl, or dialkylaminoalkyl,

each of R_2 and R'_2, independently, is hydrogen, alkyl, alkoxyalkyi, hydroxyalkyl, C_1-C_3alkylthio, S(O)C_1-C_3alkyl, CF_3;

R_3 is hydrogen or CH_3CO—; and

each of R_4, R'_4, R_5, R'_5, R_6, R'_6, R_7 and R'_7, independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, --$COO(C_1$-C_3alkyl), CF_3, nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3alkylthio, or $S(O)C_1$-C_3alkyl;

and compounds of formula III are



III

wherein

R'_1 is hydrogen, C_1-C_4alkyl, aminoalkyl, monoalkylaminoalkyl, or dialkylaminoalkyl;

R'_2 is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, C_1-C_3alkylthio, $S(O)C_1$-C_3alkyl, CF_3

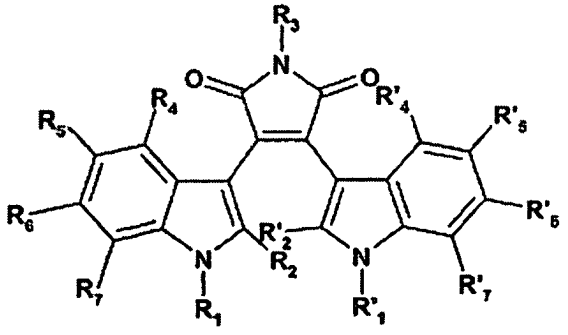
R_3 is hydrogen or CH_3CO—;

each of R_4, R'_4, R_5, R'_5, R_6, R'_6, R_7 and R'_7, independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, —$COO(C_1$-C_3alkyl), CF_3, nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3alkylthio, or $S(O)C_1$-C_3alkyl;

X is CR_8R_9 wherein R_8 is $(CH_2)_sR_{10}$ wherein R_9 is $(CH_2)_sR_{11}$, each of R_{10} and R_{11}, independently, is hydroxy, alkoxy, carboxy, acyloxy, amino, monoalkylamino, dialkylamino, trialkylamino, azido, acylamino, alkoxycarbonyl, cyano, amidino, or aminocarbonyl, and s is 0, 1, 2 or 3; and

r is 1, 2, or 3; and

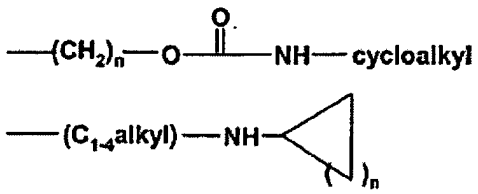
and compounds of formula IV are



IV

wherein

R_1 at is alkylglycose residue or a group of formula (g) or (h)



wherein n is 1, 2, 3, 4, 5 or 6;

R'_1 is hydrogen, C_1-C_4alkyl, cyclopropylmethyl, aminoalkyl, monoalkylaminoalkyl, or, dialkylaminoalkyl;

each of R_2 and R'_2, independently, is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, C_1-C_3alkylthio, S(O)C_1-C_3alkyl, CF_3;

R_3 is hydrogen or CH_3CO—; and

each of R_4, R'_4, R_5, R'_5, R_6, R'_6, R_7 and R'_7, independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, --COO(C_1-C_3alkyl), CF_3, nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3alkylthio, or S(O)C_1-C_3alkyl.

Claim 2 (currently amended): A method according to claim 1 for the treatment ~~or prevention~~ of an autoimmune disease wherein the autoimmune disease is selected from an inflammatory bowel disease amyotrophic lateral sclerosis; multiple sclerosis; rheumatoid arthritis and hepatitis C.

Claim 3 (currently amended): A method according to claim 1, for the treatment ~~and prevention~~ of organ or tissue transplant rejection or for the prevention of graft-versus-host disease.

Claim 4 (previously presented): A method according to claim 1 wherein the protein kinase C inhibitor is a compound of formula Ia, Ib, IIa, IIIa or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 5 (previously presented): A method according to claim 1 wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione, or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 6 (currently amended): A pharmaceutical composition for use in the treatment ~~and prevention~~ of organ or tissue transplant rejection and for the prevention of graft-versus-host disease and/or of autoimmune diseases <u>other than diabetes mellitus, said composition</u> comprising a protein kinase C inhibitor of formula I, II, III or IV as defined in claim 1 or a pharmaceutically acceptable salt, hydrate or solvate thereof, together with one or more pharmaceutically acceptable diluents or carriers therefor.

Claim 7 (previously presented): A composition according to claim 6 wherein the protein kinase C inhibitor is a compound of formula Ia, Ib, IIa, IIIa or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 8 (previously presented): A composition according to claim 6 wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 9 (previously presented): A pharmaceutical combination comprising a) a protein kinase C inhibitor of formula I, II, III or IV as defined in claim 1, or a pharmaceutically acceptable salt, hydrate or solvate thereof, and b) at least one second agent selected from an immunosuppressant and immunomodulatory drug.

Claim 10 (previously presented): A pharmaceutical combination comprising a) a protein kinase C inhibitor of formula Ia, Ib, IIa, or IIIa as defined in claim 1, or a pharmaceutically acceptable salt, hydrate or solvate thereof and b) at least one second agent selected from an immunosuppressant and immunomodulatory drug.

Claim 11 (Canceled)

Claim 12 (previously presented): A method according to claim 2 wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione, or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 13 (previously presented): A method according to claim 3 wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione, or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 14 (previously presented): A pharmaceutical combination according to claim 10 wherein a) is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione.